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09/580,523	05/30/2000	Xiao-Mai Zhou	A7483	8284

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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/580,523	ZHOU, XIAO-MAI	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-62 and 81-108* is/are pending in the application.

4a) Of the above claim(s) *31-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 71-80.

Accordingly, claims 81-108 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER

Claims 80-83, 85-93, 95-103, 105-108 remain rejected under 112, first paragraph, as the specification does not contain a written description of the claimed "an amino acid conservative for Alanine" to replace the serine 118 of the human BAD SEQ ID NO:1, for reasons already of record in paper of 08/25/05.

Applicant argues that the recitation of an amino acid conservative for alanine would be understood to be inherent.

Applicant argues that the specification discloses that substitution at Ser118 of SEQ ID NO:1 with Alanine promotes cell death, whereas Ser118 substitution with an amino acid that is not Alanine or an amino acid conservative for alanine (Aspartic acid, containing an acidic side chain) results in loss of pro-apoptic acitivity (Figure 12(c) of the instant application). Applicant argues that thus one would have recognized that amino acid conservative for Alanine would have the same apoptosis-promoting function as Alanine when placed at position 118 of SEQ ID NO:1.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

Contrary to Applicant's arguments, an amino acid conservative for Alanine is not inherent.

It is noted that figure 12(c) of the instant application does not disclose any substitution of Ser118 with a conservative substitution of Alanine. Figure 12(c) only discloses replacement of Ser155 of mouse BAD SEQ ID NO:2, which is equivalent to Ser118 of human BAD SEQ ID NO:1 (see table 1 on page 41 of the instant application), with Alanine, or Aspartic acid (S155D), which is not a conservative substitution of Alanine, but which has an acidic side chain and mimics the negatively charged phospho-Ser155 (p.89, second paragraph).

Further, one cannot predict whether conservative substitution of Alanine would still produce the same apoptosis-promoting property as Alanine when placed at position 118, because not any conservative substitution would retain the original activity of the parent polypeptide. For example, Straub P et al, 1993, J Biol Chem 268(29): 21997-20003, teach that conservative substitutions of valine for glycine at positions 111 and 117 of cytochrome P450 2C2 result in about 50- and 7-fold reduction of activity, respectively. Kouklis PD et al, 1993, J Cell Science, 106(pt 3): 919-28, teach that a single exchange of glycine 450 of the intermediate filament protein vimentin with valine strongly interfers with the normal assembly of the intermediate filaments.

Thus, a conservative substitution for Alanine at position 118 of SEQ ID NO:1 is not an inherent property, and one would conclude that the specification lacks support for a conservative substitution for Alanine at position 118 of SEQ ID NO:1.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 81-108 remain rejected under 35 USC 112, second paragraph, for the use of the language "the position corresponding by sequence alignment" with SEQ ID NO:1 to position 118 of SEQ ID NO:1, for reasons already of record in paper of 08/225/05.

Applicant argues that "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is clearly defined in the specification, and that serine is not alanine or an amino acid conservative for alanine.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

The term "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is not defined in the specification, nor limiting (see detail discussion below, under Written description).

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 81-108 remain rejected under 35 USC 112, first paragraph, for lack of a clear written description of a polypeptide "comprising" an amino acid sequence that is identical or could have at least "75%, 85% or 90% sequence identity" with amino acids

114-122, or 103-123, or 106-132 of SEQ ID NO:1, wherein the amino acid at "the position corresponding by sequence alignment" with SEQ ID NO:1 to position 118 of SEQ ID NO:1 is Alanine, or an amino acid conservative for Alanine, or is not Alanine, or is not Glycine, wherein said polypeptide has at least one in vitro activity selected from the group consisting of cell death promoting activity, Bcl-XL binding activity and Bcl-2 binding activity, and wherein the polypeptide could be at least 10 or 25 amino acid long, for reasons already of record in paper of 08/25/05.

A) The claims encompass variants of full length SEQ ID NO:1.

Applicant argues that a "reference point" is not needed in order to align two sequences. Applicant argues that the entire sequence, rather than a single amino acid, is used to align one sequence with another.

Applicant argues that "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is clearly defined in the specification with regard to any of the homologues and fragments encompassed by the present claims. Applicant argues that for example, the specification describe how sequence alignment allows identification of regions of sequence homology, in particular, the identification of Serine or other amino acid, at a position corresponding to Serine at position of SEQ ID NO:1, by the alignment of the sequence of mutant BAD or fragment of a mutant BAD with SEQ ID NO:1 (p.9, 41, 45, 50). Applicant argues that Table 1 at page 41 illustrates how sequence alignment can be used to identify the position corresponding to 118 of SEQ ID NO:1 in the mouse BAD sequences, which vary slightly from SEQ ID NO:1.

Applicant argues that what is conventional in the art or well known in the art need not be disclosed in detail. Applicant argues that the sequence alignment is well known in the art, and described in numerous references.

Applicant argues that the Examiner uses the sequence alignment in the 102(e) rejection, and yet at the same time maintains that one would not know which amino acid is referred to by the term amino acid position corresponding by sequence alignment to position of SEQ ID NO:1.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

Contrary to Applicant's arguments, the term "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is not defined in the specification, nor limiting.

The specification only discloses on pages 9, 41, 45, 50 that the position 118 of SEQ ID NO:1, or the BH3 domain of SEQ ID NO:1 is determined by using sequence alignment. Table 1 on page 41 shows the results of the alignment. In other words, the specification does not define sequence alignment, but only discloses the results of sequence alignment.

Although the technique of sequence alignment is known in the art, however, In view of a lack of a definition of the term "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1", the term "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" encompasses any amino acid of a sequence to be aligned with

SEQ ID NO:1, using any of numerous ways of alignment. For example an unknown sequence is placed side by side with SEQ ID NO:1, wherein any amino acid position of said unknown sequence could be the reference point and is aligned with the first amino acid or any amino acid of SEQ ID NO:1, and the rest of the unknown sequence is place side by side with SEQ ID NO:1, using said reference point for alignment of the unknown sequence with SEQ ID NO:1.

In conclusion, because one cannot determine which amino acid is the reference point for sequence alignment in the claims, any amino acid could correspond by sequence alignment to position 118 of SEQ ID NO:1.

Further, even if the only Alanine substitution is at position 118 of SEQ ID NO:1, due to the language "comprises" and due to the fact that amino acids 114-122, or 103-123, or 106-132 of SEQ ID NO:1 are only fragments of SEQ ID NO:1, the claims unknown sequences attached to amino acids 114-122, or 103-123, or 106-132 of SEQ ID NO:1, wherein amino acid position 118 of said amino acids 114-122, or 103-123, or 106-132 of SEQ ID NO:1 is Alanine.

Thus the claims encompass variants of SEQ ID NO:1, with unknown structure, provided they have at least "75%, 85% or 95% or 100% sequence identity" with amino acids 114-122, or 103-123, or 106-132 of SEQ ID NO:1.

For the reasons set forth above, and in previous Office action, **there is no correlation between the structure of the claimed sequences and the function of cell death promoting activity, or Bcl-XL or Bcl-2 binding activity. Further, the described single variant of human BAD polypeptide of SEQ ID NO:1, wherein**

amino acid position Ser118 is replaced with Ala118, and two variants of the murine BAD polypeptides of SEQ ID NO:2 and 3, wherein the equivalent Serine at positions 155 and 113, respectively, is replaced with Alanine, are not representative species.

Thus the claims and the specification fail to describe the claimed variant BAD polypeptides, by the standard shown in the examples of Lilly and Enzo, and one of skill in the art would conclude that Applicant did not have possession of the claimed genus of BAD variant polypeptides at the time the invention was made.

B. The claims also encompass variants of SEQ ID NO:1 comprising a variant BH3 domain, or a fragment thereof.

Applicant argues that the BH3 domain was so well characterized at the time the invention was made that one would have been able to predict the specific mutation within the BH3 domain would have on function of the peptide.

Applicant recites Zha et al, 1997, Kelekar et al, 1997, and Sattler et al, 1997.

Applicant argues that the articles demonstrate the use of sequence alignments to indicate primary sequence homology between the critical BH3 domains of BAD and other apoptosis regulators of the BCL-2 family. Applicant argues that functional mutants of BAD can be designed by analogy to other well studied members of the BCL-2 family. Applicant argues that the crystal structure of BAK was known at the time of the filing date of the instant application. Applicant argues that Sattler et al test the binding affinity of numerous mutant BAK BH3 containing peptides, and demonstrate that the BAK

peptide adopts an amphipathic alpha-helix that interacts with BCL-XL through hydrophobic and electrostatic interaction.

Applicant argues that Fig2B of Zha et al shows the predicted structure of the BH3 amphipathic alpha-helix of BAD, providing views of the hydrophobic and polar surfaces, and indicating the likely positions of the amino acid residues.

Applicant argues that Zha et al also use site-directed mutagenesis to substitute individual amino acids within the BH3 region of BAD, and assess the effect of the various mutations on both in vitro and in vivo heterodimerization with Bcl-XL and on cell death promoting activity (Figures 5 and 6).

The recitation of Zha et al, 1997, Kelekar et al, 1997, and Sattler et al, 1997 is acknowledged and entered.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

Contrary to Applicant's arguments, at the time of filing of the instant application, the art does not teach which and/or how many amino acids of the BAD BH3 region actually could be substituted, added, or deleted, without affecting the function of promoting cell death of dephosphorylated BAD.

One cannot extrapolate from the structure-function study of BAK, to the function of the claimed variant BAD BH3. Although BAK, similar to BAX and BAD, is a death agonist, and binds to Bcl-2 or BCl-XL via its BH3 domain (Kelelar et al, 1997, Mol Cell Biol, 17(12): 7040-7046, especially p.7040, second column, second paragraph), BAK is a different molecule from BAD, with different BH3 amino acid composition, sharing with

BAD in the BH3 region only two amino acids 151L and 156D (Zha et al, 1997, JBC, 272(39): 24101-24104, especially figure 2A on page 4). The only similarity is that both probably have amphipathic alpha-helix structure. Since BAK BH3 is different in structure and would have different amino acid interactions with BCL-XL and BCL-2 than BAD BH3 , thus BAK BH3 cannot used to extrapolate to the function of the claimed variant BAD BH3.

Further, although Fig2B of Zha et al shows in a the predicted possible structure of the BH3 amphipathic alpha-helix of mouse BAD (amino acids 151-163), providing views of the predicted hydrophobic and polar surfaces, and indicating the likely positions of the amino acid residues, it is only a model and not an actual crystal structure or NMR analysis. Only Leu151 in the mouse BAD BH3 domain was actually shown to be critical for the binding to Bcl-XL and Bcl-2 (Zha et al, p.5, last paragraph). Which other amino acids of the BAD BH3 region actually are critical contact sites with Bcl-XL or Bcl-2 are not disclosed, nor predicted, especially in view of the comment by Zha et al that 1) substitution of Gly 149 of mouse BAD affects its binding to Bcl-2 much more than to Bcl-XL, indicating a difference in the contact sites of these anti-apoptotic molecules, i.e. in view of such difference, one does not know which of the amino acids of the hydrophobic and polar surfaces of BAD are contact sites with Bcl-XL, and which of the amino acids of the hydrophobic and polar surfaces of BAD are contact sites with Bcl-2, and 2) BAD is more closely related to BID and BIK than to BAK (p.8, second and last paragraphs). It is further noted that not all alpha-helix BH3 domains have the same preference or properties, i.e. the same critical contact sites; for example, a BID BH3

domain prefers binding to BAK and BAX, whereas the BAD BH3 domain prefers binding to Bcl-2 (Letai et al, of record, p.184, second column, first paragraph), and similarly, while the BAD BH3 and BID BH3 domains alone could trigger apoptosis (Letai et al, of record, p.188, second column), the BH3 domain alone of the polypeptides that also have also BH1 and/or BH2 domain, such as BCL-XL, BAX or BAK, does not always induce apoptosis (Letai et al, of record, p.190, first column, second paragraph).

Thus, except for a single amino acid, Leu 151, of mouse BAD BH3, one cannot predict the effect of any other mutations in the BAD BH3 domain would have on the function of BAD.

The claims however encompass a sequence comprising variant BH3 domain, wherein except for Ser 118A in the human BAD, SEQ ID NO:1, any other amino acids in the BAD BH3 domain could have any deletion, addition or substitution with any amino acid.

It is noted that Applicant's cited reference, Kelekar et al, 1997, Mol cell Biol, 17(12): 7040-7046, actually confirms the reasons for rejection by the Examiner. It is noted that the mouse BAD BH3 domain comprises 26 amino acids at positions 140-165 of mouse BAD SEQ ID NO:2 (Kelekar et al, table 1 on p.7043, and Letai et al, of record, table 1 on page 184), which is equivalent to amino acids 103 to 129 of human BAD, SEQ ID NO:1 (the instant specification, table 1 on page 41). Thus the claimed polypeptides consisting of amino acids 114-122, 103-123, or 106-132 of SEQ ID NO:1, or of at least 10, or 25 amino acids long represent the human BAD variants with deletion, or addition at either terminus. Whether the function of which is retained could

not be predicted. Kelekar et al teach that a portion of mouse BAD BH3, the 16-mer amino acids 145-160 of SEQ ID NO:2, which is equivalent to amino acids 108-123 of human BAD, SEQ ID NO:1, does not significantly bind to Bcl-XL (table 1 on page 7043). Further, **Kelekar et al went on and teach that BAD functions by dimerizing with Bcl-XL, and that determination of the specific residues involved in dimerization can come only from a resolution of the structure of the Bcl-XL-BAD 26-mer complex, accompanied by point mutational analysis (i.e. single base pair mutation) of this region** (p.7045, second column, second pargraph).

In view of such unpredictability, **there is no correlation between the structure of the claimed sequences and the function of cell death promoting activity, or Bcl-XL or Bcl-2 binding activity. Further, the described single variant of human BAD polypeptide of SEQ ID NO:1, wherein amino acid position Ser118 is replaced with Ala118, and two variants of the murine BAD polypeptides of SEQ ID NO:2 and 3, wherein the equivalent Serine at positions 155 and 113, respectively, is replaced with Alanine, are not representative species.**

Thus the claims and the specification fail to describe the claimed variant BAD polypeptides, by the standard shown in the examples of Lilly and Enzo, and one of skill in the art would conclude that Applicant did not have possession of the claimed genus of BAD variant polypeptides at the time the invention was made.

C) The function of binding to BCL-XL or Bcl-2 is not a definitive function, that defines the claimed BAD polypeptide, and does not correlate with the

structure of BH3 domain, in view that BAX binds to Bcl-2 via its BH1 or BH2 domain (Yin et al, 1994, of record).

Applicant asserts that the recitation of Bcl-XL or Bcl-2 binding has been deleted.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

The recitation of Bcl-XL or Bcl-2 binding has not been deleted.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 81-108 remain rejected under 35 USC 112, first paragraph, because the specification, while being enabled for a polypeptide comprising SEQ ID NO:1, wherein its Serine amino acid at position 118 is replaced with Alanine, and wherein said polypeptide has in vitro cell death promoting activity, does not reasonably provide enablement for any variant polypeptide of SEQ ID NO:1, for reasons already of record in paper of 08/25/05.

Applicant argues that because the structure and function of the BH3 domain of BAD and other related proteins had been extensively analyzed, one would know how to design mutant polypeptides that would retain the cell death promoting activity. Applicant argues that one could identify the claimed variants because any assay for determining cell death promoting activity in vitro is described in the specification.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

Concerning Applicant's arguments that because the structure and function of the BH3 domain of BAD and other related proteins had been extensively analyzed, one would know how to design mutant polypeptides that would retain the cell death promoting activity, this issue has been discussed above, under Written description.

Further, one would not know how to make the claimed variant polypeptides, in view that protein chemistry is unpredictable, and that a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of the protein, as taught by Bowie, Burgess et al, lazar et al, Tao et al, and Gillies et al, all of record, and further in view that the mutated BH3 domain of BID, having two amino acids substitutions at L90A and D95A, losses the ability to induce apoptosis, as taught by Letai et al, of record.

Moreover, one cannot predict that a variant BAD polypeptide, wherein amino acid position 118 of SEQ ID NO:1 could be any amino acid, other than Alanine or Glycine, could promote cell death, in view that when Ser118 of SEQ ID NO:1 is replaced with Aspartic acid, to mimic the negatively charged phosphoserine 155 residue, no pro-apoptotic activity is found (the instant application, p.89, second paragraph).

In view of such unpredictability, it would be undue experimentation for one of skill in the art to screen for the claimed variant BAD polypeptide.

Further, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays, and by inference suggestions of structural analysis, are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

REJECTION UNDER 35 USC 102 (e)

Claims 81-108 remain rejected under 35 USC 102(e) as being anticipated by US 5,965,703, for reasons already of record in paper of 08/25/05.

Applicant argues that "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is clearly defined in the specification, and that serine is not alanine or an amino acid conservative for alanine.

Applicant's arguments in paper of 11/25/05 have been considered but are found not to be persuasive for the following reasons:

The term "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position 118 of SEQ ID NO:1" is not defined in the specification, nor limiting, supra (see detail discussion above, under Written description).

Thus the claimed polypeptides seem to be the same as the prior art human BAD polypeptide, which is 100% similar to SEQ ID NO:1 of the claimed invention, and which promotes cell death, and binds to human Bcl-XL or Bcl-2.

Moreover, even if the corresponding amino acid is serine 118 of SEQ ID NO:1, claims 85-86, 95-96, 105-106 are anticipated by the wild type human BAD polypeptide taught by US 5,965,703, because the amino acid position 118 could be any amino acids other alanine, or glycine, e.g. serine in the polypeptide taught by the art, and thus the claimed polypeptide clearly is the same as the art polypeptide.

Although the reference does not specifically teach a polypeptide, wherein "the amino acid position corresponding by sequence alignment with SEQ ID NO:1 to position

118 of SEQ ID NO:1" is alanine, or a conservative thereof, or is not alanine or is not glycine, however, the claimed polypeptide appears to be the same as the prior art polypeptide. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

December 22, 2005